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EXAMINER	
KINGAN, TIMOTHY G	

ART UNIT	PAPER NUMBER
1797	

NOTIFICATION DATE	DELIVERY MODE
12/14/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/519,014	FLANDRE ET AL.	
	Examiner	Art Unit	
	TIMOTHY G. KINGAN	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/07/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

Applicant's arguments with respect to claim 1 have been considered but are moot in view of the new ground(s) of rejection. With regard to claim 10, applicant melds intended use language in the apparatus claim, specifically with regard to the use of a capacitance detector and the circuitry thereof for detecting conductive labels, the labels themselves not being integral to the device or claimed in a system comprising both device and labeled targets. The Courts have held that if the prior art structure is capable of performing the intended use, then it meets the claim. Apparatus claims must be distinguishable from the prior art in terms of structure, not function. The manner of operating an apparatus does not differentiate an apparatus claim from the prior art, if the prior art apparatus teaches all of the structural limitations of the claim (see MPEP § 2114 & § 2173.05(g)). However, examiner notes Ewart teaches that reporters used in the capacitance sensor may be metals (conductive labels), the sensor including the electrodes is passivated (rendering the electrodes non-conducting), and the sensor incorporates a Wheatstone Bridge (sensing circuitry). The claim as written is met by the teachings of Ewart.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. **Claims 10-13, 17, 21-25 and 27** are rejected under 35 U.S.C. 102(b) as being anticipated by T.G. Ewart and T. Bogle, U.S. Patent 5,922,537 (herein after Ewart).

For Claim 10, Ewart teaches capacitive biosensors with a test surface (col 14, lines 10-11) (sensor comprising a substrate) for detecting particles of metals, polymers, glasses, phages and the like (col 1, lines 1-12; Table 1) (target sample), such particles functioning as reporters or labeling entities for target analytes in a sample (col 3, line 66 to col 4, line 9) (metals acting as reporters are conductive labels), biosensors comprising electrodes (col 16, lines 23-25) the surfaces of which are passivated (insulated/surfaces made non-conductive in region of binding site) with silicon nitride (col 14, lines 54-56; col 16, lines 28-30) or parylene polymer (col 14, lines 2-4) and coated with silica to facilitate covalent linking of molecules (able to selectively bind a capacitive sensor element). Further, a sensor may comprise an interdigitated electrode (Fig. 14; col 15, lines 31-33) (at least two electrodes) in which capacitances are measured with a sensing circuit (a capacitive sensor element) comprising a Wheatstone Bridge (col 18, lines 44-54; Fig. 10) (circuitry arranged in a manner fully capable for determining the presence of conductive labels between electrodes).

For Claim 11, Ewart teaches measuring differential capacitance related to addition or removal of particles that alter the conductive properties of the test surface (col 9, lines 13-21 and col 5, lines 18-21) (conductive labels coupled to target sample).

For Claim 12, Ewart teaches a pair of electrodes, each comprising an array of interdigitated fingers (array of parallel fingers), each pair of electrodes (anodes and cathodes) being individually addressed (Fig. 1).

For Claim 13, Ewart teaches a thin film device for capacitance measurements comprising coplanar interdigitated capacitor plates (col 15, lines 31-33; data: Fig. 14) (all fingers of an anode or cathode being short-circuited).

For Claim 17, Ewart teaches a capacitive sensor comprising semiconductor substrate functionalized to react with amino silanes (col 6, lines 59-62).

For Claim 21, Ewart teaches a Wheatstone Bridge circuit for measuring differential changes in sensor capacitance (a comparator unit) (col 18, lines 40-47; Fig. 10).

For Claim 22, Ewart teaches a capacitive sensor with a phosphorescence sensor (optical detector) comprising an optical waveguide for focusing light on the phosphorescence detector (col 17, lines 47-50).

For Claim 23, Ewart teaches a capacitive biosensor with the use of magnetic particles as labels for targets, the presence of such particles being measured as a change in inductance (col 2, lines 16-19) (a magnetic sensor).

For Claims 24 and 27, Ewart teaches a capacitive sensor with electrodes made of titanium (a non-noble metal) with or without a gold metallization layer (col 14, lines 50-52).

For Claim 25, Ewart teaches a capacitive sensor, the mini-wells between electrodes being coated with a dielectric layer (non-conducting surface) of silicon nitride (col 16, lines 26-30).

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. **Claims 1-5 and 9** are rejected under 35 U.S.C. 103(a) as being unpatentable over T.G. Ewart and T. Bogle, U.S. Patent 5,922,537 (herein after Ewart) in view of S-J. Park et al., Science, 295: 1503-1506, 2002.

For Claims 1-3, Ewart teaches biosensors with a test surface (a substrate) and their use in hybridization assays for detecting particles of metals (conductive labels), polymers, glasses, ceramics and phages (abstract, col 1, lines 5-11), such detection methods based on properties of the particles or their contribution to phenomena such as capacitance which are measured in the method (col 1, lines 55-57; col 14, lines 10-11; col 15, lines 20-22). In the detection method of Ewart, a fluid is applied and a second analyte is bound to a first analyte which itself is irreversibly affixed to the substrate, the second analyte labeled with reporter particles (col 2, lines 49-53) (binding a target sample to selective binding sties on the substrate).

With regard to the step of detecting the presence of conducting labels using electrodes having non-conducting surfaces, Ewart does not specifically teach use of conductive labels as reporters in the method; however, Ewart does teach detecting

particles of metals, polymers, glasses, phages and the like (col 1, lines 1-12; Table 1) (target sample), such particles functioning as reporters or labeling entities for target analytes in a sample (col 3, line 66 to col 4, line 9) (metals acting as reporters are conductive labels), biosensors comprising electrodes (col 16, lines 23-25), the surfaces of which are passivated (insulated/surfaces made non-conductive in region of binding site) with silicon nitride (col 14, lines 54-56; col 16, lines 28-30) or parylene polymer (col 14, lines 2-4) and coated with silica to facilitate covalent linking of molecules (able to selectively bind a capacitive sensor element). It would have been obvious to one of ordinary skill in the art to use conductive labels in capacitive detection, and with reasonable expectation of success, according to the teaching of Ewart on use of metals in reporter labels and their contribution to measurements of capacitance, since the presence of such labels would alter the dielectric of the medium comprising the gap between detecting electrodes.

Ewart also does not specifically teach non-ohmic contact in the method of detecting capacitance changes. Examiner notes that in semiconductor technology, a non-ohmic circuit comprises a type of resistive circuit yielding a non-linear response in current to changes in voltage (a normal ohmic circuit yields a linear response), such as with a diode; if a different or additional meaning of "non-ohmic contact" is intended by applicant, such meaning is not disclosed. The limitation is therefore examined by treating such term to mean non-conductive or capacitive contact, as through an electric field. In this context, Ewart does teach reporters are in contact with electrodes via their electric field, a contact not comprising a change in conductance or resistance, and

therefore, non-ohmic (e.g., Fig. 8). Further, Park teaches a method of electrically detecting gold nanoparticle-labeled (abstract) (conductive labels) nucleic acid hybrids comprising the step of immobilizing capture oligonucleotides on an activated surface of a substrate (p. 1504, ¶ 2) and then exposing to nanoparticle-labeled probe oligonucleotides (p. 1504, ¶ 3) (binding target sample to selective sites, labeled with conductive labels, to determine presence of hybrids). The method of Park does not specifically teach capacitive sensing, rather, detection of changes in resistance; however, Park does teach that, in principle, capacitance measurements can be made (p. 1503, ¶ 2).Therefore, the teaching of Ewart on measurement of capacitance using metal reporters with a device comprising non-conducting electrodes together with Park's suggestion for such measurement of capacitance in the greater context of measurements of resistance with gold-labeled targets, falls within the scope of the claim. From the combined teachings, such measurement would have been obvious to one of ordinary skill in the art.

Ewart's method further comprises determining a base level signal (a preliminary capacitance measurement) and comparing such signal with a test signal (col 3, lines 2-4) (sensing the presence of labels).

Further with regard to sensing step, Ewart teaches said biosensors comprise electrodes (col 16, lines 23-25), the surfaces of which are passivated with silicon nitride (col 14, lines 54-56; col 16, lines 28-30) or parylene polymer (col 14, lines 2-4) (electrodes having non-conductive surfaces) and coated with silica to facilitate covalent

linking of molecules (creating selective binding sites on the sensor substrate for affixing first analyte to which second analyte in target sample will bind).

For Claims 4-5, Ewart does not teach enlarging of labels prior to or during the sensing step. Park teaches a method of detection comprising treatment of bound label with silver enhancer solution (p. 1504, ¶ 3) during which metallic silver is deposited at nucleating nanoparticle sites (labels enlarged by silver precipitation prior to the sensing step) (Fig. 3). It would have been obvious to one of ordinary skill in the art to use such silver enhancement to ensure reducing or bridging of the gap between non-conductive electrodes of Ewart with conductive label in order to provide control or enhancement of the reactance of the electrode surface in signal detection by altering the dielectric of the medium.

For Claim 9 Ewart teaches use of magnetic properties of particles to be detected (col 1, lines 55-57 and col 2, lines 13-19).

3. **Claims 6 and 7** are rejected under 35 U.S.C. 103(a) as being unpatentable over Ewart in view of Park as applied to claim 1 above, and further in view of C. Berggren et al., Electroanalysis 13(3): 173-180, 2001.

For Claim 6, Ewart and Park are silent on measurement of capacitance as a function of frequency. However, such use of frequency in detection of capacitance is known in the art. Berggren teaches capacitive biosensors in which impedance spectra are obtained by measurements at different AC frequencies (p. 179, ¶ 1). It would have been obvious to one of ordinary skill in the art to use measurements at different

frequencies in order to characterize an unknown system within the method of Ewart and Park to optimize the capacitive contribution to impedance, and, in so doing optimize parameters of the measurement for detecting changes in the dielectric.

For Claim 7, Ewart and Park do not teach measurement of global impedance. Berggren teaches measurement of both in-phase (real part) and out-of-phase impedance (p. 176, ¶ 1) (together, global impedance) and the affects of non-specific binding on in-phase impedance (using the real part of global impedance) (p. 176, ¶ 1). It would have been obvious to one of ordinary skill in the art to separately consider the two components of impedance within the teaching of Berggren in order to distinguish between capacitive changes associated with non-specific binding and binding or hybridization of labeled target to probe and to use such information in optimizing the experimental conditions of binding steps in the method of Park, thereby increasing specificity and sensitivity.

4. **Claim 8** is rejected under 35 U.S.C. 103(a) as being unpatentable over Ewart in view of Park as applied to claim 1 above, and further in view of T.A. Taton et al., Science 289: 1757-1760, 2000.

For Claim 8, Ewart and Park are silent on use of optical detection. Taton teaches a method of detection of gold nanoparticle-labeled targets (conductive labels) hybridized to probe immobilized on a biosensor comprising the use of a flatbed scanner (optical detection) (Fig. 1 and caption). It would have been obvious to one of ordinary skill in the art to use optical detection according to the teaching of Taton within the method of

Ewart and Park in order to provide for detection with simple and inexpensive equipment that is capable of high spatial and gray-scale resolution and is commonly available in laboratories.

5. **Claim 14** is rejected under 35 U.S.C. 103(a) as being unpatentable over Ewart as applied to claim 10 above, and further in view of M. Taguchi et al., U.S. Patent Application Publication 20020050173 (herein after Taguchi).

For Claim 14, Ewart is silent on electrodes as an array of crossed fingers. However, such arrays are known in the art, for instance in pressure-sensitive transducers. Taguchi teaches electrodes comprising electrodes in which at least one electrode portion crosses a plurality of electrode portions of opposite polarity [0006]. One of ordinary skill in the art would find obvious to use such arrays according to the teaching of Taguchi in the device of Ewart for increasing the spatial resolution in transducing signal associated with changing resistance or capacitive component of impedance. Further, one of ordinary skill in the art would find desirable such increase in resolution in order to separately address multiple reactive sites with a single array of crossed fingers.

6. **Claim 15** is rejected under 35 U.S.C. 103(a) as being unpatentable over Ewart as applied to claim 10 above, and further in view of M. DeSilva et al., Biosensors and Bioelectronics 10: 675-682, 1995 (herein after DeSilva).

For Claim 15, Ewart is silent on electrodes as a matrix of points. However, such configurations for detecting probe-target interactions are known in the art. DeSilva teaches a biosensor for use in antigen-antibody interaction comprising a discontinuous film of platinum islands (matrix) of 60-120 Å diameter as electrodes on a silicon dioxide substrate (p. 677, ¶ 1), and that such arrangement is extremely sensitive to small changes in electrical properties of the material (analyte) between the islands. One of ordinary skill would find obvious from the teaching of DeSilva the use and desirability of such islands in order to detect changes in impedance (capacitive component thereof) associated with lower affinity events of antigen-antibody interaction or nucleic acid hybridization.

7. **Claim 16** is rejected under 35 U.S.C. 103(a) as being unpatentable over Ewart as applied to claim 10 above, and further in view of C. Berggren and K-M. Chang et al., U.S. Patent 6,236,096 (herein after Chang).

For Claim 16, Ewart is silent on a three electrode capacitive sensor. Such three electrode systems are known in the art and permit measurement of two capacitance values, including that from a sensor and a second from a reference. Berggren teaches a three electrode system for detecting capacitance changes in biosensors (p. 178, ¶ 6). Further, Chang teaches capacitive pressure sensor with a three-prong electrode (col 1, ¶ 1). One of ordinary skill in the art would find obvious to use such three electrode system according to the teachings of Berggren and Chang in the sensor of Ewart in

order to provide for local calibration in capacitance, since variations in manufacture across the sensor would degrade resolution in high sensitivity measurements.

8. **Claim 18** is rejected under 35 U.S.C. 103(a) as being unpatentable over Ewart as applied to claim 10 above, and further in view of G.T.A. Kovacs, U.S. Patent 6,682,936 (herein after Kovacs).

For Claim 18, Ewart is silent on the use of the conductive label as a gate for a MOS- or EEPROM-like structure. Kovacs does not teach a conductive label creating a MOS gate but does teach an array of electrodes on an integrated circuit chip for carrying out multi-step biochemical reactions, an electrode of which is formed above a MOS-photodiode structure within a CMOS circuit (embedded in the semiconductor below the binding sites) (col 4, lines 22-26, col 9, lines 56-60 and Fig. 7). It would have been obvious to one of ordinary skill in the art to use a conductive label as a gate for MOS transducer according to the teaching of Kovacs within the sensor of Ewart in order to provide the advantages in electronic stability of an on-board switch in the circuitry associated with detecting a reaction or binding event.

9. **Claims 19-20** are rejected under 35 U.S.C. 103(a) as being unpatentable over Ewart as applied to claim 10 above, and further in view of P. Van Gerwen et al., International Conference on Solid-State Sensors and Actuators Chicago, June 16-19, p. 907-910, 1997 (herein after Van Gerwen).

For Claim 19, Ewart is silent on the spacing of electrodes with respect to the size of a single label. Ewart teaches nanoparticles for use in biosensors having diameters

less than 1000 nanometers. Van Gerwen teaches spacings of fingers in interdigitated electrodes used in biochemical sensors of 250 nanometers (p. 907, ¶ 3). Knowing the range of spacing available for configuring electrodes, one of ordinary skill in the art would have found obvious to optimize the size of nanoparticles, commercially available in a range of diameters, in order to match or fall under that of the electrode spacing, depending on the need for resistive (calling for a short circuit between electrodes) or capacitive measurements or capacitive component of impedance measurements.

For Claim 20, Ewart and Van Gerwen are silent on the distance between two electrodes. One of ordinary skill in the art would find obvious to optimize such distance (d in $C=\varepsilon\varepsilon_0 A/d$, the expression for capacitance) in order to provide for optimal signal in capacitance, since such property is inversely proportional to d and the effective value will change with a change in the dielectric associated with the presence of nanoparticles.

10. **Claim 26** is rejected under 35 U.S.C. 103(a) as being unpatentable over Ewart in view of N. Maruno et al., U.S. Patent 5,917,264 (herein after Maruno) and J. Vangrunderbeek et al., U.S. Patent 6,514,394 (herein after Vangrunderbeek).

For Claim 26, Ewart does not teach use of aluminum electrodes or non-conductive surface formed by alumina. Such materials are known for use in fabrication of electrodes and non-conducting surfaces of electrodes in sensors. N. Maruno teaches a pressure sensor with aluminum electrodes (col 14, lines 45-47) and J. Vangrunderbeek teaches a sensor in which the non-conducting material is made of

alumina (col 8, lines 23-24. It would have been obvious to one of ordinary skill in the art to use aluminum for electrodes in order to obtain the advantage of readily available foil for which the thickness and area (and therefore, capacitance) can be easily controlled and to use alumina for non-conducting surfaces in order to provide the advantage available in manufacture associated with vapor deposition.

Conclusion

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY G. KINGAN whose telephone number is

(571)270-3720. The examiner can normally be reached on Monday-Friday, 8:30 A.M. to 5:00 P.M., E.S.T.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TGK /Jill Warden/
Supervisory Patent Examiner, Art Unit 1797